

Segm fold from 1/2

1 GAAGTGCAGCGGGGTGGATTTCCTGGAATTGCCTTAGTAGTAGTACCACCCAAGGCAC TG
61 CTTAGGTACCAC TGTGCTTAGTGGAGAGTCCCTCTGGCTTTATCATTAAAGGTTTTGGGC
121 GGAAAGACGTAGTTGAATATTTGCTTCAGAATGGTGCAAATGTCCAAGCACGTGATGATG
181 GGGGCCCTTATTCTCTTCATAATGCATGCTCTTTTGGTCATGCTGAAGTAGTCAATCTCC
241 TTTTGCGACATGGTGCAGACCCCAATGCTCGAGATAATTGGAATTATACTCCTCTCCATG
301 AAGCTGCAATTAAAGGAAAGATTGATGTTTTGCATTGTGTGCTATTTTGCAGTGCTGTTA
361 CAGCATGGAGCTGAGCCAACCATCCTAAATACAGATGGAAGGACAGCATTGGATTTAGCA
421 GATCCATCTGCCAAAGCAGTGCTTACTGGTGAATATAAGAAAGATGAACTCTTAGAAAGT
481 GCCAGGAGTGGCAATGAAGAAAAAATGATGGCTCTACTCACACCATTAAATGTCAACTGC
541 CACGCAAGTGATGGCAGAAAGTCAACTCCATTACATTTGGCAGCAGGATATAACAGAGTA
601 AAGATTGTACAGCTGTTACTGCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGAT
661 CTGGTACCATTACACAATGCCGTGTTCTTATGGTCATTATGAAGTAACTGAACTTTTGGTC
721 AAGCATGGTGCCTGTGTAAATGCATGGACTTGTGGCAATTCACCTCTCTTATGAGGCA
781 GCTTCTAAGAACAAGGGTTGAAGTATGTTCTCTTCTTAAGTTATGGTGCAGACCCAACA
841 CTGCTCAATTGTCACAATAAAAGTGCTATAGACTTGGCTCCCACACCACAGTTAAAGAA
901 AGATTAGCATATGAATTTAAAGGCCACTCGTTGCTGCAAGCTGCACGAGAAGCTGATGTT
961 ACTCGAATCAAAAAACATCTCTCTCTGGAATGGTGAATTTCAAGCATCCTCAAACACAT
1021 GAAACAGCATTGCATTGTGCTGCTGCATCTCCATATCCCAAAAGAAAGCAAATATGTGAA
1081 CTGTTGCTAAGAAAAGGAGCAAACATCAATGAAAAGACTAAAGAATTCTTGACTCCTCTG
1141 CACGTGGCATCTGAGAAAGCTCATAATGATGTTGTTGAAGTAGTGGTGAACATGAAGCA
1201 AAGGTTAATGCTCTGGATAATCTTGGTCAGACTTCTCTACACAGAGCTGCATATTGTGGT
1261 CATCTACAAACCTGCCGCCCTACTCCTGAGCTATGGGTGTGATCCTAACATTATATCCCTT
1321 CAGGGCTTTACTGCTTTACAGATGGGAAATGAAAATGTACAGCAACTCCTCCAAGAGGGT
1381 ATCTCATTAGGTAATTCAGAGGCAGACAGACAATTGCTGGAAGCTGCAAAGGCTGGAGAT
1441 GTCGAAACTGTAAAAAACTGTGTACTGTTTCAGAGTGTCAACTGCAGAGACATTGAAGGG
1501 CGTCAGTCTACACCAC TTCATTTTGCAGCTGGGTATAACAGAGTGTCCGTGGTGGAAATAT
1561 CTGCTACAGCATGGAGCTGATGTGCATGCTAAAGATAAAGGAGGCCTTGTACCTTTGCAC
1621 AATGCATGTTCTTATGGACATTATGAAGTTGCAGAACTTCTTGTTAAACATGGAGCAGTA
1681 GTTAATGTAGCTGATTTATGGAAATTTACACCTTTACATGAAGCAGCAGCAAAAGGAAAA
1741 TAGGAAATTTGCAAACTTCTGCTCCAGATGGTGCGAGACCTTACCAAAAAAACAAGGGAT
1801 GGAAATACTCCTTTGGATCTTGTGTTAAAGATGGAGATACAGATATTACATTATCTGCTTAGG
1861 GGAGATGCAGCTTTGCTAGATGCTGCCAAGAAGGGTTGTTTAGCCAGCATGAAGAAGTTG
1921 TCTTCTCCTGATAATGTAATTTGCCGCGATACCCAAGGCAGACATTCAACACCTTTACAT

1981 TTAGCAGCTGGTTATAATAATTTAGAAGTTGCAGAGTATTTGTTACAACACGGAGCTGAT
 2041 GTGAATGCCCAAGACAAAGGAGGACTTATTCCTTTACATAATGCAGCATCTTACGGGCAT
 2101 GTAGATGTAGCAGCTCTACTAATAAAGTATAATGCATGTGTCAATGCCACGGACAAATGG
 2161 GCTTTCACACCTTTGCACGAAGCAGCCCCAAAAGGGACGAACACAGCTTTGTGCTTTGTTG
 2221 CTAGCCCATGGAGCTGACCCGACTCTTAAAAATCAGGAAGGACAAACACCTTTAGATTTA
 2281 GTTTCAGCGGATGATGTGTCAGCGCTCTTCTGACAGCAGCCATGCCCCATCTGCTCTGCCC
 2341 TCTTGTTACAAGCCTCAAGTGCTCAATGGTGTGAGAAGCCCAGGAGCCACTGCAGATGCT
 2401 CTCTCTTCAGGTCCATCTAGCCCATCAAGCCTTTCTGCAGCCAGCAGTCTTGACAACTTA
 2461 TCTGGGAGTTTTTCAGAACTGTCTTCATTAGTTAGTTCAAGTGGAACAGAGGGTGCTTCC
 2521 AGTTTGGAGAAAAAGGAGGTTCCAGGAGTAGATTTTAGCATAACTCAATTCGTAAGGAAT
 2581 CTTGGACTTGAGCACCTAATGGATATATTTGAGAGAGAACAGATCACTTTGGATGTATTA
 2641 GTTGAGATGGGGCACAAGGAGCTGAAGGAGATTGGAATCAATGCTTATGGACATAGGCAC
 2701 AAACATAATTAAGGAGTCGAGAGACTTATCTCCGACAACAAGGTCTTAACCCATATTTA
 2761 ACTTTGAACACCTCTGGTAGTGGAACAATTCTTATAGATCTGTCTCCTGATGATAAAGAG
 2821 TTTCACTCTGTGGAGGAAGAGATGCAAAGTACAGTTCGAGAGCACAGAGATGGAGGTCAT
 2881 GCAGGTGGAATCTTCAACAGATACAATATTCTCAAGATTGAGAAGGTTTGTAACAAGAAA
 2941 CTATGGGAAAGATACACTCACCGGAGAAAAGAAGTTCTGAAGAAAACCACAACCATGCC
 3001 AATGAACGAATGCTATTTTCATGGGTCTCCTTTTGTGAATGCAATTATCCACAAAGGCTTT
 3061 GATGAAAGGCATGCGTACATAGGTGGTATGTTTGGAGCTGGCATTATTTTGTGTAAGAAC
 3121 TCTTCCAAAAGCAATCAATATGTATATGGAATTGGAGGAGGTACTGGGTGTCCAGTTCAC
 3181 AAAGACAGATCTTGTTACATTTGCCACAGGCAGCTGCTCTTTTGGCGGGTAACCTTGGGA
 3241 AAGTCTTTCTGTCAGTTTCAGTGCAATGAAAATGGCACATTCTCCTCCAGGTCATCACTCA
 3301 GTCAGTGGTAGGCCCAGTGTAATGGCCTAGCATTAGCTGAATATGTTATTTACAGAGGA
 3361 GAACAGGCTTATCCTGAGTATTTAATTACTTACCAGATTATGAGGCCTGAAGGTATGGTC
 3421 GATGGATAAATAGTTATTTTAAAGAACTAATCCACTGAACCTAAAATCATCAAAGCAGC
 3481 AGTGGCCTCTACGTTTTACTCCTTTGCTGAAAAA

ref|NP_003738.1|PTNKS| TANKYRASE >gi|3929219 (AF082556) TRF1-interacting
 ankyrin-related

ADP-ribose polymerase [Homo sapiens] Length = 1327
 Score = 1640 bits (4199), Expect = 0.0

Identities = 790/1023 (77%), Positives = 871/1023 (84%), Gaps = 11/1023 (1%)
 Query: 35 VLLQHGAEPITLNTDGRALDLADPSAKAVLTGEYKKDELLESARSGNEEKMALLTPLN 94
 VLLQHGA+P I NTDG++ALDLADPSAKAVLTGEYKKDELLE+ARSGNEEK+MALLTPLN
 Sbjct: 300 VLLQHGAADPNIRNTDGKSALDLADPSAKAVLTGEYKKDELLEAARSGNEEKLMAALLTPLN 359
 Query: 95 VNCHASDGRKSTPLHLAAGYNRVKIVQLLLQHGADVHAKDKGDLVPLHNACSYGHYEVT 154
 VNCHASDGRKSTPLHLAAGYNRV+IVQLLLQHGADVHAKDKG LVPLHNACSYGHYEVT
 Sbjct: 360 VNCHASDGRKSTPLHLAAGYNRVIVQLLLQHGADVHAKDKGGLVPLHNACSYGHYEVT 419
 Query: 155 LLVKHGACVNAMDLWQFTPLHEAASKNRVEVC SLLLSYGADPTLLNCHNKSALDLAPTPQ 214
 LL+KHGACVNAMDLWQFTPLHEAASKNRVEVC SLLLS+GADPTL+NCH KSA+D+APTP+
 Sbjct: 420 LLLKHGACVNAMDLWQFTPLHEAASKNRVEVC SLLLSHGADPTLVNCHGKSADVMAPTPE 479
 Query: 215 LKERLAYEFKGHSLLQAAREADVTRIKKHSLEMVNFKHPQTHETALHCAAASPYPKRKQ 274
 L+ERL YEFKGHSLLQAAREAD+ ++KK L+LE++NFK PQ+HETALHCA AS +PKRKQ
 Sbjct: 480 LRERLTYEFKGHSLLQAAREADLAKVKKTLALEI INFKQPQSHETALHCAVASLHPKRKQ 539
 Query: 275 ICELLLRKGANINEKTKEFLTPLHVASXXXXXXXXXXXXXXXXXXXXLDNLGQTS LHRAA 334
 + ELLLRKGAN+NEK K+F+TPLHVA+ LD LGQT+LHRAA
 Sbjct: 540 VTELLLRKGANVNEKNKDFMTPLHVAAERAHNDVMEVLHKHGAKMNAALDTLGQTALHRAA 599
 Query: 335 YCGHLQTCRLLLSYGCDPNIIISLQGF TALQMGNE NVQQLLQEGISLGNSEADRQLLEAAK 394
 GHLQTCRLLLSYG DP+IISLQGF TA QMGNE VQQ+L E + S+ D +LLEA+K
 Sbjct: 600 LAGHLQTCRLLLSYGSDPSIIISLQGF TAAQMGNEAVQQILSESTPIRTSDVDYRLLEASK 659

Query: 395 AGDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQHGADVHAKDKGGLV 454
 AGD+ETVK+LC+ Q+VNCRD+EGR STPLHFAAGYNRVSVVEYLL HGADVHAKDKGGLV
 Sbjct: 660 AGDLETVKQLCSSQNVNCRDLEGRHSTPLHFAAGYNRVSVVEYLLHHGADVHAKDKGGLV 719

Query: 455 PLHNACSYGHYEVAELLVKHGAVNVADLWKFTPLHEAAAKGKYEICKLLLQHGDPTKK 514
 PLHNACSYGHYEVAELLV+HGA VNVADLWKFTPLHEAAAKGKYEICKLLL+HGADPTKK
 Sbjct: 720 PLHNACSYGHYEVAELLVRHGASVNVADLWKFTPLHEAAAKGKYEICKLLLKHGADPTKK 779

Query: 515 NRDGNTPLDLVKDGDTDIHYXXXXXXXXXXXXXXXXXXXXRVKKLSSPDNVNCRDTQGRHST 574
 NRDGNTPLDLVK+GDTDI RV+KL +P+N+NCRDTQGR+ST
 Sbjct: 780 NRDGNTPLDLVKEGDTDIQDLLKGDAALLDAAKKGCLARVQKLCTPENINCRDTQGRNST 839

Query: 575 PLHLAAGYNNLEVAEYLLQHGADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNAT 634
 PLHLAAGYNNLEVAEYLL+HGADVNAQDKGGLIPLHNAASYGHVD+AALLIKYN CVNAT
 Sbjct: 840 PLHLAAGYNNLEVAEYLLLEHGADVNAQDKGGLIPLHNAASYGHVDIAALLIKYNTCVNAT 899

Query: 635 DKWAFTPLHEAAQKGRTQLCALLLAHGADPTLKNQEGQTPLDLVSADDVSALLTAAMPPS 694
 DKWAFTPLHEAAQKGRTQLCALLLAHGADPT+KNQEGQTPLDL +ADD+ ALL AMPP
 Sbjct: 900 DKWAFTPLHEAAQKGRTQLCALLLAHGADPTMKNQEGQTPLDLATADDIRALLIDAMPPE 959

Query: 695 ALPSCYKPQ---VLNGVRSPGATXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX 751
 ALP+C+KPQ V + SP +T
 Sbjct: 960 ALPTCFKPQATVVSASLISPAST-----PSCLSAASSIDNLTGPLAELAVGGASNAG 1011

Query: 752 XXXXXXXXXXXKKEVPGVDFSITQFVRNLGLEHLMDIFEREQITLDVLVEMGHKELKEIGIN 811
 + EV G+D +I+QF+++LGLEHL DIFE EQITLDVL +MGH+ELKEIGIN
 Sbjct: 1012 DGAAGTERKEGEVAGLDMNISQFLKSLGLEHLRDFEFETEQITLDVLADMGHEELKEIGIN 1071

Query: 812 AYGHRHKLIGVERLISGQQGLNPYLTLNTSGSGTILIDLSPDDKEFQSVEEEMQSTVRE 871
 AYGHRHKLIGVERL+ GQQG NPYLT + GTIL+DL+P+DKE+QSVEEEMQST+RE
 Sbjct: 1072 AYGHRHKLIGVERLLGGQQGTNPYLTFHCVNQGTILLDLAPEDKEYQSVEEEMQSTIRE 1131

Query: 872 HRDGGHAGGIFNRYNLIKIQVCNKKLWERYTHRRKEVSEENHNHANERMLFHGSPFVNA 931
 HRDGG+AGGIFNRYN+++IQKV NKKL ER+ HR+KEVSEENHNH NERMLFHGSPF+NA
 Sbjct: 1132 HRDGGNAGGIFNRYNVIRIQVNVNKKLRERFCHRQKEVSEENHNHNERMLFHGSPFINA 1191

Query: 932 IIHKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYGIGGGTGCPVHKDRSCYICHRQLLF 991
 IIHKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYGIGGGTGCP HKDRSCYICHRQ+LF
 Sbjct: 1192 IIHKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYGIGGGTGCPVHKDRSCYICHRQMLF 1251

Query: 992 CRVTLGKSFLQFSAMKMAHSPPGHHSVTGRPSVNGLALAEYVIYRGEQAYPEYLITYQIM 1051
 CRVTLGKSFLQFS MKMAH+PPGHHSV GRPSVNGLA AEYVIYRGEQAYPEYLITYQIM
 Sbjct: 1252 CRVTLGKSFLQFSTMKMAHAPPGHHSVIGRPSVNGLAYAEYVIYRGEQAYPEYLITYQIM 1311

Query: 1052 RPE 1054
 +PE
 Sbjct: 1312 KPE 1314

 GAAGTGCAGCGGGGTGGATTTCCTGGAATTGCCTTAGTAGTAGTACCACCCAAGGCACTG
 CTTAGGTACCACTGCTGCTTAGTGGAGAGTCCCTCTGGCTTTATCATTAAGGTTTTGGG
 CGGAAAGACGTAGTTGAATATTTGCTTCAGAATGGTGCAAATGTCCAAGCACGTGATGAT
 GGGGGCCTTATTCCTCTTCATAATGCATGCTCTTTTGGTCATGCTGAAGTAGTCAATCTC
 CTTTTCGACATGGTGCAGACCCCAATGCTCGAGATAATTGGAATTATACTCCTCTCCAT
 GAAGCTGCAATTAAAGGAAAGATTGATGTTTGCATTTGTGTGCTATTTTGCAGTGTGT
 TACAGCATGGAGCTGAGCCAACC
 ATCCTAAATACAGATGGAAGGACAGCATTTGGATTTAGCAGATCCATCT

Exhibit B

09/863, 169

w/ Tank northern
blob

→ This slide is for Jaseen

Chk1 two-hybrid screening

Bait: Chk1

is a protein kinase required for cell cycle arrest in response to DNA damage

Hit: a novel protein homology to ATP-dependent RNA helicase
belongs to the DEAD-box RNA helicase family

The fission yeast *cdc28(+)* encodes a member of the DEAD-box family of putative RNA helicases involved in pre-mRNA splicing and cell cycle progression

a new gene encoding a putative DEAD box helicase have been isolated to suppress uncontrolled mitosis by overexpression *cdc25* in fission yeast
(Chk1 and 14-3-3 proteins also show up in this screening)

It is interesting to characterize the interaction of Chk1 and the novel RNA helicase and its role in cell cycle control

Potential targets for further pursuing

p21 hit:	Tankyrase homolog
Traf4 hit:	Cdk liked kinase
hRad9 hit:	PP5
PNCA hits:	a novel helicase a human homolog of SNM1 a novel endo/exo-ribonuclease
Chk1 hit:	an ATP-dependent RNA helicase homolog

Target validation:

- full length cloning
- examine the RNA expression in tumor verse normal tissues
- peptide binding library screening in YTH---->functional assay
- generate dominant-negative mutant

p21 hit: a Tankyrase homolog

Tankyrase (a poly(ADP-ribose) polymerase at human telomeres)

- a protein with homology to ankyrin and to the catalytic domain of ADP-ribose polymerase (PARP)
- is localized to human telomeres
- binds to the telomeric protein TRF1 (telomeric repeat binding factor-1)
- is a positive regulator of telomere length maintenance

TITLE _____

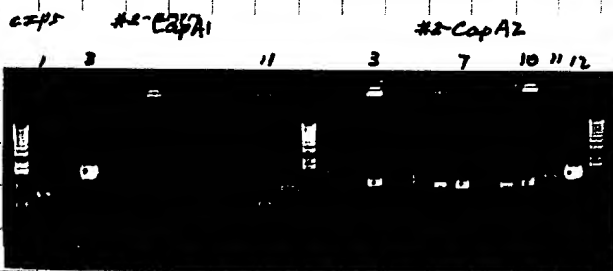
From Page No. _____

Repeat 1P but use N/A primer
 PCR primer: N/A RII N/A
 templates: N/A (AT) 1P
 N/A (AT) 2P
 Cap30. 2'10" X



7/13 ② #2-CapA1 & #2-CapA2

✓ PCR insert screening primer: N/A/RII

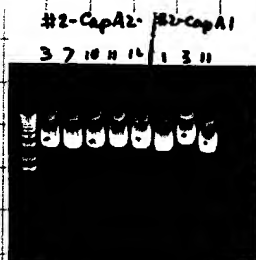


7/19 ① screening more



7/14 ③

mini plasmid prep



#2-CapA2-3 (N/A)
 -10
 -12

#2-CapA1-3
 -11

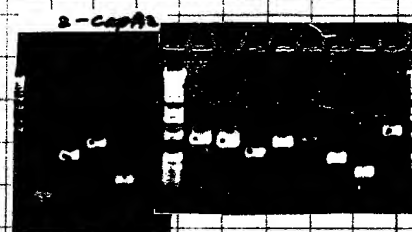
300ng each

Result
 no sequence

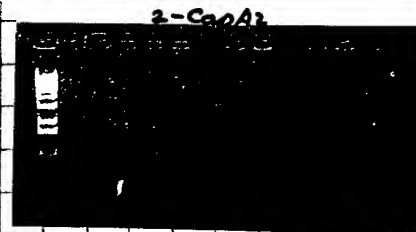
7/14 ③
 to sequence

isoform 1
 isoform 3

7/12

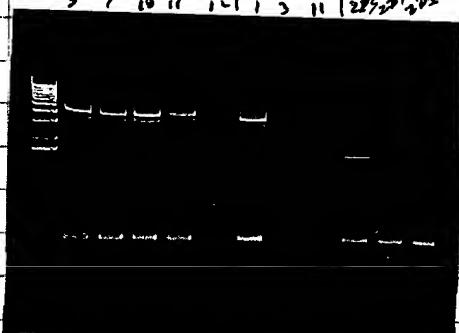


FB/RII check



#2, per check FB/RII!

#2-CapA2- 3 7 10 11 12 | #2-CapA1- 1 3 11 | 28/29/30/31



mini. 7/10

To Page No. 137

Witnessed & Understood by me,

JH

Date

8/27/99

Invented by

RS

Recorded by

RS

Date

7/13/99

From Page No. 115

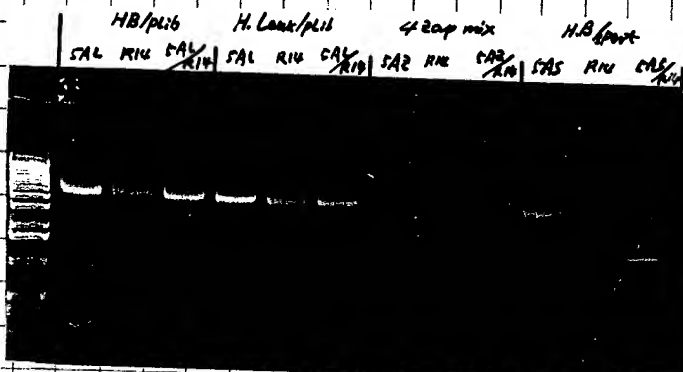
7/1/99 ① 5'-end cloning.

from library.

Template:

- ① HB/plib primer
 ② H. Leuk/plib
 ③ 4zap mix
 ④ HB/psport
- SAL/R14
 "
 SA2/R14
 SAS/R14

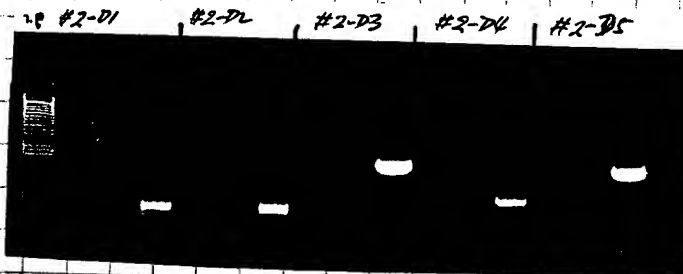
Gap30 (2'10")



7/13/99 ②

2P
 5B/R11 5B/R11
 #2-D1
 2 3 4 5
 Cap23

GP GP GP GP
 #2-D1 (SAL/R14) #2-D2 (SAL/R14) #2-D3 (SAL/R14) #2-D4 (SAS/R14)
 #2-D2 " " " " " " " "
 insert screening
 2-D3, 2-D4 only
 T/A cloning & 2P



7/14

PCR insert screening, primer 5B2/R11

GP GP GP GP GP
 #2-E1 (5B2/R11) #2-E2 (5B2/R11) #2-E3 (5B2/R11) #2-E4 (5B2/R11) #2-E5 (5B2/R11)
 X X X X X
 To sequence 7/14 ②
 AT/A cloning
 Check insert with F13/R11 (11)

PCR insert screening, primer 5B2/R11

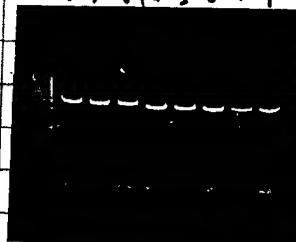
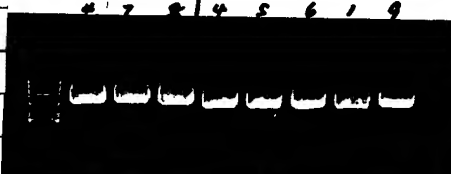


7/15 ③

mini prep

2ul on gel
cath

Cotc = 300 uA



Witnessed & Understood by me,

Date

Invented by

Date

To Page No. _____

Recorded by

7/17/99

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TITLE

pcmt40 #4.

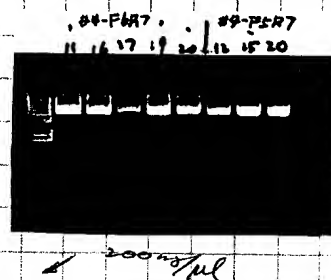
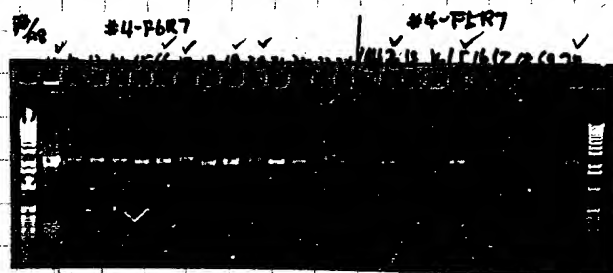
Project No. _____

Book No. _____

127

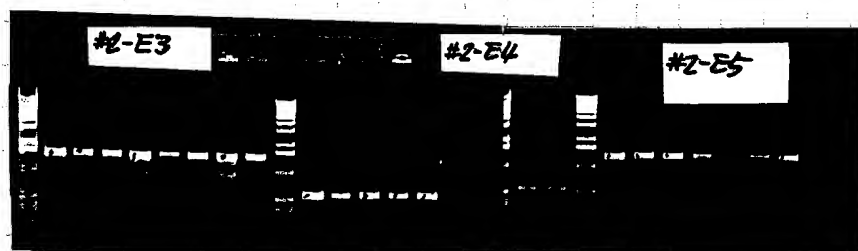
From Page No. 121

7/12/99 ① per insert screening again (last time the amount clones are not enough)
primer use FS/R8



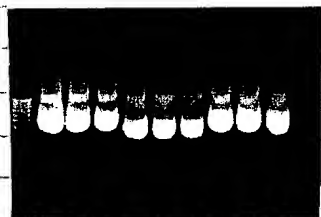
#4-F6R7-11 } 7/13
-19 } to sequence
-20 }
#4-F5R7-18 }

7/15/99 Clones per insert screening



↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓

↓ mini (7/14)



7/20/99 ① 7/13/RU insert check result: all of them have band.

To Page No. _____

Witnessed & Understood by me,

JH

Date

8/1/99

Invented by

S1

Recorded by

S2

Date

7/13/99

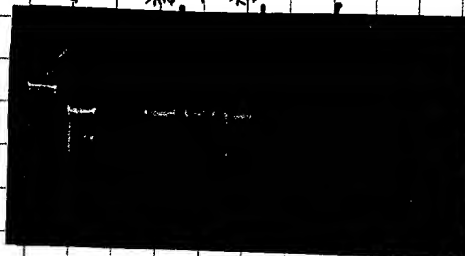
From Page No. 124

7/1/99 (2) Compare pH of PCR Buffer.

API R14 API R14
 Template H₂O (Marathon) 300µl 1. in 25 µl PCR
 + 0.5 µl 1 M HCl + 0.2 µl 1 M HCl
 + 1.5 µl " + 0.5 µl "
 + 2.1 µl " + 0.8 µl "

Cap30
nonuseful

HCl 0 0.2 µl 0.5 µl 0.8 µl
 API R14 API R14 API R14 API R14



X

Try New buffer & API.

API R14 API R14

API R14 API R14 API R14 API R14
 New Buffer
 Primer 3



X

Witnessed & Understood by me,

JH

Date

8/2/99

Invented by

GJ

Recorded by

GJ

Date

7/15/99

To Page No. _____

7/6/97 (1997) (2-5-) (page date) (change) (sequence)

1. ~~HB~~ { T+B X 6/25, p111 } Boek kit X #2-B4-1 (1997) X
 H. leuk/pl V (R14, R11) clontech kit V -3
 -4

2. { HBCR V 6/30, p115-7 } #2-C1-6 (1997)
 T+B V R14 (HB) -7
 -12
 -18
 H. Mala X #2-C2-1 (1997) V
 (HB) -5
 #2-C3-11 (1997) V
 (HB) -12
 -18

3. { HB/pl V 7/2, p126-7 } X HB too small 90% mini & clones
 H. leuk/pl V R14 15% → but didn't pass F13/R11 check X
 4 Zap mix → ∴ no to sequencing
 H.B/ps V X too more colony plate give per 100 to R14
 #2-D3 (H. leuk)
 #2-D4 (4 Zap mix)
 #2-D5 (HB/pl)

2. ~~HB~~ myself X 7/2, p122, 128 X primer & adaptor problem
 HB R14 Normal Prot. different PH but C. New buffer

3. clontech Marathon Ready cDNA, 7/6, p119
 { H. Fetal Brain X
 H. Fetal Liver X
 H. Leukocyte X

3. ~~HB~~ 7/9, p14-5
 { HB primed V
 HB, R14 X

#2-CapA1-3 (1997) V isoform 1
 -11 (0.5 kb) V isoform 3
 #2-CapA2-3 (1997)
 -10
 -12 (1.2 kb) V no seq

(Mass F13/R11 check)
 #2-CapA1-29 (1997) V
 -33 (1.2 kb) V
 -34 (2.2 kb) V
 #2-CapA2-26 (1997) V
 -29 (0.9 kb) V

Result: got 2 isoform from Smart RACE. & got isoform from Library method.
 But Marathon did work.
 7/22 finish it.

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Book No._____

137

TITLE

CZPS. #2

From Page No. 125

mini prep.	21 each
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$\sim \text{conc} = 200 \text{ ng}/\mu\text{L}$



- F13/R11 insert check again.

2-CapA-29

33

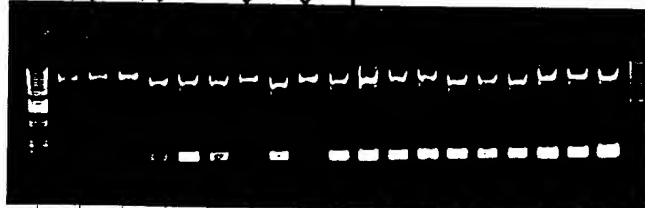
344

to sequence $7/20$ (2)

2-CapA2-26

-29

11-2-2011
CIP5



7/21 (3) pick 20 clones from #2-CapA1

PCR insert screening. NUP/RH & F13/RH



N/R	per
-------	-----

41 43



~~Род. 12. 12. 1900~~

№2 - Cap Al-50

(N/RU)

#2-62A1-00

1	min
---	-----

(See p/35)

#2-CapA1-60 to sequence (7/22)

To Page No.

Witnessed & Understood by me,

၂၈

Date _____

8/17/99

Invented by

Recorded by _____

54

55

Date

7/21/99

RIGEL

4931

FLEHR, HONBACH, TEST
ALBRITTON & HERBERT

1999 JUL 22 AM 9:02

RECEIVED

July 20, 1999

RIGEL, INC.

VIA FEDERAL EXPRESS

Ms. Robin Silva
Flehr, Hobach, Test, Albritton, & Herbert
4 Embarcadero Center, Suite 3400
San Francisco, California 94111-4187

Per RMS - OPEN
AS USING

Re: Provisional Patent Applications.

Dear Ms. Silva,

Per Brian Cunningham's request, enclosed with this letter are eight packages of information generated by Dr. Ying Luo in preparation for provisional patent application filings. Each package pertains to a different genetic sequence that Rigel believes may be commercially useful. Each package contains relevant scientific materials, journal references and abstracts of proposed gene functions.

Please file a provisional patent application for each document.

If you have any questions, please call me at 650-624-1106.

Respectfully yours,

Nicole Verona

Nicole A. Verona
Rigel Pharmaceuticals, Inc.

Exhibit DE 09/843,149



FLEHR, HOBACH, TEST
ALBRITTON & HERBERT

1999 JUL 23 AM 10:04

RECEIVED

July 22, 1999

RIGEL, INC.

VIA FEDERAL EXPRESS

Ms. Robin Silva
Flehr, Hobach, Test, Albritton, & Herbert
4 Embarcadero Center, Suite 3400
San Francisco, California 94111-4187

*ORIGINAL Diskette in
P-68287*

Re: Provisional Patent Applications.

Dear Ms. Silva,

It was a pleasure to meet you today. I'm sorry that I did not see you leave; I had intended to give you these diskettes before the end of our meeting.

On these diskettes are the documents that we reviewed earlier. The new document that Ying gave to me today will be ready on Monday.

If you have any questions, please call me at 650-624-1106.

Respectfully yours,

Nicole Verona

Nicole A. Verona
Rigel Pharmaceuticals, Inc.

Exhibit # F 09/843,149

DOCKETING/BILLING SYSTEM FILE INFORMATION
(Patent/Design Patent)

Date: July 26, 1999 File No.: A-68292
Client: Rigel Pharmaceuticals Access Code: 4931
Client Attorney: DJB/RMS/DAV
Ref. No.:

New ☒ Update ☐ Close ☐
Parent ☐ Div. ☐ CPA ☐ CIP ☐

Subject Description

Title: TANKYRASEH, A Cell Cycle Protein

Inventors: Ying Luo

Serial No.:
Filing Date:

Patent No.:
Issue Date:

Assignee:

Related Files:

If Foreign file, please provide corresponding U.S. Serial Number
or Patent Registration Number.

Misc. (Include any action items and due dates here!):

Submitted by: Gail Clark Date: July 26, 1999

cc: Accounting
Docketing - Foreign
Docketing - US

BEST AVAILABLE COPY

Exhibit AG 09/843, 149

From: Nicole Verona <NVerona@rigel.com>
To: "'dvance@flehr-iplaw.com'" <dvance@sfpo.fhtah.fleh...
Date: 8/30/99 4:01pm
Subject: FW: FW: info

Dear Dolly,

I forwarded your questions to Ying Luo and this is the response I received from him. I hope this helps. Also, I've got copies of the TNIK manuscript figures that you need. Would you like me to fax them to you?

Nicole

-----Original Message-----

From: Ying Luo [mailto:yluo@rigel.com]
Sent: Sunday, August 29, 1999 2:44 PM
To: Nicole Verona
Subject: Re: FW: info

2868 PAN is from PCNA screening. tankyraseH is from CIP screening. CIP is also called p21. R0101 has an entry in GenBank with full length sequence with a name called KIAA0101. No functional annotation about R0101. PP5 was cloned and published before. The novelty is we can link PP5 to RAD9, a cell cycle checkpoint control protein. You should have all figures of TNIK manuscript already. TNIK nucleotide sequences are attached. PAN nucleotide sequence is already in Genbank.

Ying

At 03:21 PM 8/26/99 -0700, you wrote:

>Hi Ying!

>

>Here are some of the questions I need to discuss with you.

>

>Nicole

>

>-----Original Message-----

>From: Dolly Vance [mailto:dvance@flehr-iplaw.com]
>Sent: Friday, August 20, 1999 1:42 PM
>To: nverona@rigel.com
>Subject: info

>

>

>Dear Nicole,

>Hope you're well. Here's a complete list of what I am missing from the

>initial 9 disclosures.

>

>1) The names of binding partners (if any actual) for CAH and
>tankyraseH.

>2) The nucleic acid and amino acid sequences for PAN and TNIK
>(actually, all figures that go with the manuscript for TNIK).

>3) Please confirm that R0101 and PP5 are NOT novel, and that all
>others are novel.

>

>Thanks. Dolly

>P.S. I understand your hours are reduced. Any chance you can give me a

>time frame for providing the above information? Thanks again, Dolly

>

RIGEL™

RIGEL, INC.

FLEHR, HOHBACH, TEST
ALBRITTON & HERBERT

1999 OCT -1 AM 10:09

RECEIVED

Exhibit H 09/843 149

September 30, 1999

Ms. Dolly Vance
Flehr, Hohbach, Test, Albritton and Herbert LLP
4 Embarcadero Center, Suite 3400
San Francisco, California 94111-4187

Dear Dolly,

Enclosed are documents pertaining to the cell-cycle patent applications that you requested.

The documents include:

1. TankyraseH abstracts involving TRF, P21, and PARP
2. TankyraseH nucleotide sequence alignment report
3. TankyraseH amino acid sequence alignment report
4. R0101 figures with corrected CDK 2, 3, and 4 labels
5. Mkinase nucleotide and amino acid sequences with its kinase domain and nuclear localization sequence (NLS) highlighted

Additional information will be sent to you next week.

Please call or email me if you have any questions.

Sincerely,

Nicole Verona

Nicole Verona